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Bovine Spongiform Encephalopathy: Implications for the United States

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Bovine Spongiform Encephalopathy: Implications for the United States

Bovine spongiform encephalopathy (BSE), a fatal degenerative neurological disease of cattle, was first recognized in Great Britain (GB) in November 1986, and has since affected approximately 100 thousand cattle. Animal health officials in GB have hypothesized that this new disease resulted from exposure of cattle to a scrapie-like agent in ruminant-origin feeds containing meat and bone meal (MBM). In GB the incidence of BSE among dairy herds is 10 times that among beef herds. The risk of BSE increases with herd size; however, the within-herd incidence is low, with the majority of herds experiencing less than three cases. Although BSE has reached epidemic proportions only in GB, it has occurred in native-born cattle in the Republic of Ireland, France, and Switzerland. BSE has also been found in Oman, the Falkland Islands, and Denmark in cattle imported from the United Kingdom (UK). The importation of ruminants from countries with BSE was banned by the U.S. in July 1989. BSE has not been diagnosed in the U.S.

This report contains four articles relating to BSE:

A series of questions and answers describes BSE in GB; the current status of the epidemic as well as epidemiologic and research findings. Indications are that the July 1988 ban on the feeding of ruminant-derived proteins to ruminants is beginning to have the desired effect.

A brief review of the current BSE status in Great Britain supports the initial hypothesis that linked BSE to the consumption of scrapie-infected meat and bone meal. Risk factors for BSE in the U.S. were initially proposed by USDA:APHIS:VS in 1990. Changes within each of the risk factors are evaluated. It was concluded that since there was either no change or a decrease in the magnitude of risk factors, the overall risk of BSE in the U.S. has decreased.

Components of BSE surveillance in the U.S. are described. A primary component of active surveillance is the histologic examination of cattle brains. It is estimated that, since BSE has not been found in a sample of 1,215 brains examined, the maximum potential prevalence of BSE in the U.S. is between 3.9 per 100,000 and 1.3 per million total adult cattle. Passive surveillance includes the analysis of existing data sources for spatial or temporal patterns. The network of private practitioners who refer unusual cases to veterinary medical schools or State diagnostic laboratories provides an important informal detection system.

Nonambulatory cows have been proposed as a source of a spongiform encephalopathy in mink. A preliminary assessment of this association is based on a small, nonrandom survey of dairies in select States. The survey suggested that almost 5,000 nonambulatory cows suspect of having a transmissible spongiform encephalopathy (TSE) could have been fed to mink in the surveyed States in 1992. Given the potentially large number of nonambulatory cows fed to mink and the historically sporadic occurrence of spongiform encephalopathy in mink, it was concluded that if a TSE exists in U.S. cattle, then it is very rare or the conditions for its transmission to mink must be highly specific.

An Update on Bovine Spongiform Encephalopathy in Great Britain

July 1993

1. What is the current status of the BSE epidemic?

    * Worldwide, over 100,000 laboratory confirmed cases of BSE.

    * As of July 2, 1993, over 99 percent (100,581) of laboratory confirmed cases have occurred in Great Britain. Within Great Britain:

        * Twenty-seven (27) percent of all farms have experienced at least one case (45 percent of all dairy farms and 9 percent of all beef farms).

        * On affected farms, 41 percent have experienced only one case, 70 percent have experienced less than 3 cases.

2. What is the current status of spongiform encephalopathies in other species within Great Britain?

    * Sixteen (16) confirmed cases in exotic animals (13 in exotic ruminants, 3 in exotic felines).

    * Forty-two (42) confirmed cases in cats, no known cases in dogs.

    * No confirmed cases of spongiform encephalopathies within Cervidae, despite feeding of ruminant derived rations.

3. What is the evidence to suggest the BSE epidemic has peaked?

    * The number of new herds experiencing BSE cases has fallen off.

    * The number of cases confirmed per month has stopped rising.

    * The total number of cases observed is lower than the number forecast in the absence of control measures.

    * BSE incidence in animals born since 1988 is decreasing.

    * Substantial decreases in the number of newly diagnosed BSE cases are expected in 1994 and beyond as the ruminant-derived meat and bone meal feed ban takes effect (since the mean age at onset of clinical signs is between 4 and 5 years).

4. Has the July 1988 ban on feeding ruminant derived animal proteins to ruminants reduced the magnitude of the Great Britain epidemic?

    * As of July 9, 1993 there have been 2,985 confirmed cases in cattle born after the feed ban.

* Over 90 percent of the 2,985 cases occurred in cattle born in 1988.

* There have been two cases in cattle born after 1989. Both cases are under further investigation.

* The age specific incidence of BSE in cattle born after the ban is less than the comparable age specific incidence of BSE in cattle born before the ban.

* The imposition of the feed ban is estimated to have prevented at least 20,000 cases in the year from April 1992 to March 1993.

5. Will the diagnostic approaches or case management change as the epidemic progresses in GB?

* As the number of BSE cases decline, the relative proportion of suspect cattle without BSE will increase. Therefore, revised protocols for examination of BSE cases may become necessary.

* Veterinary medical officers are already required to revisit BSE suspects born after the feed ban of July 1988 to further rule out alternative diagnoses before euthanizing the cow for histopathologic examination.

* Alternative post-mortem diagnostic approaches such as electron-microscopy and immunohistochemistry continue to be evaluated. To date, histopathologic examination of the obex region for vacuolation appears to be equally as sensitive and specific as electron-microscopy for identification of scrapie-associated fibrils (SAF).

6. Have the epidemiological studies generated any new information about BSE transmission or pathogenesis?

* Observations continue to be consistent with a common-source foodborne epidemic with no strong evidence to support a major role for either horizontal or vertical (maternal) transmission.

* Neither the clinical signs nor the histopathology of BSE have changed over the course of the epidemic.

* No simple genetic susceptibility factor for BSE has been identified in cattle. If there is a genetic component to susceptibility, then a high proportion of British cattle appear to be susceptible.

7. What are the latest results of the transmission studies using tissues from BSE-affected cattle?

* Under laboratory conditions, oral transmission has been achieved by feeding relatively large amounts of brain tissue to sheep, goats, mink and mice.

* The oral infective dose under natural conditions remains unknown.

* No detectable infectivity has been identified after inoculation of mice with spleen, semen, buffy coat, muscle, bone marrow, placenta, lymph nodes, cerebrospinal fluid, liver, rumen, foetal calf blood, pancreas, and proximal colon.

* No detectable infectivity has been identified after feeding mice with milk and udder, spleen, placenta, or lymph node.

8. Any advances in the antemortem diagnosis of BSE?

* Electrochemical analysis of urine has tentatively identified relative concentration differences in 3 constituents between normal cows and those with BSE.

* While this analysis of urine is not feasible for large-scale screening or cow-side testing, further analysis of the constituents is underway.

* Electrophoretic studies of cerebrospinal fluid, urine and other body fluids continue.

9. How about other studies of BSE underway at the Central Veterinary Laboratory in the UK?

* Offspring of BSE-affected cows, including embryo transfers, continue to be monitored to address questions concerning maternal transmission. Due to the long incubation period of BSE, these studies will continue 4-7 more years before the results are known.

* The pathogenesis of BSE in cattle is being evaluated by sacrifice of laboratory-exposed calves at 6 month intervals from birth. Exposure took place in December 1991.

* Infective dose and incubation are being examined by oral exposure of calves to different dosages of brain homogenate. Calves were exposed in January 1992.

* Transmission studies with oral exposure to pigs and chickens have not yet been completed.

* An epidemiological case-control study of BSE cases born after the ban is underway to address the risk of contaminated feed carryover, exposure to BSE cases or maternal transmission. Preliminary results are expected in the spring of 1994.

10. What has been the BSE disposal, compensation and research costs in Great Britain?

* Through March 1993, approximately $200 million have been spent for compensation and disposal.

* Approximately $50 million has been spent on research and development.

* Expenditures for office and field support as well as lost domestic and international markets for live animals and cattle related products have not been estimated.

11. Has BSE reduced the demand for beef within GB?

* Prior to BSE, beef consumption was on a slow downward trend.

* Early in the epidemic, beef slaughter initially declined by approximately 30 percent but then resumed to previous levels.

* BSE has not caused a long-term negative decline in overall domestic consumption.

Answers are based on personal communication with officials from the Ministry of Agriculture, Fisheries, and Food (MAFF), and the following references:

MAFF. 1993. Bovine spongiform encephalopathy in the United Kingdom - a progress report. Presented at the OIE General Assembly. May 1993. Paris, France.

Richards, M.S; Wilesmith, J.W.; Ryan, J.B.M. et al. 1993. Methods of predicting the incidence of BSE. Proceedings of the Society of Veterinary Epidemiology and Preventive Medicine. April 1993.

Wilesmith, J.W. and Ryan, J.B.M. 1993. Bovine spongiform encephalopathy: observations on the incidence during 1992. Vet Rec 132:300-301

A Review of Bovine Spongiform Encephalopathy (BSE) in Great Britain and an Update on Risk Factors for BSE in the United States

Objective

The purpose of this report is to review the current status of BSE in GB, to update the status of risk factors for BSE in the U.S., and to qualitatively evaluate changes in the risk of BSE originally proposed by the U.S. Department of Agriculture, Animal and Plant Health Inspection Services, Veterinary Services (USDA:APHIS:VS) in 1991 (1-3). At that time it was concluded that there was little evidence to support a broad risk for BSE among a large portion of the dairy population of the U.S. Since that assessment was based on data primarily from 1989, information presented in this report will be compared to 1989 data.

BSE in Great Britain

Epidemiologists in GB linked BSE to the consumption of scrapie-contaminated MBM relatively early in the course of the epidemic (4). This led, in July of 1988, to a total ban on the feeding of ruminant-derived protein to ruminants. Since the mean age at onset of clinical signs is approximately 5 years, the effect of the ban will only begin to become evident in 1993. This time lag is obscured by potentially-infected feed that remained in the supply chain or on farms after the ban. As of July 1993, a total of 2,985 cases had occurred in animals born after the ban. However, all but two of those cases had access to feed containing ruminant protein. Investigation of the two other cases continues.

Early signs indicate that the feed ban is beginning to have the desired effects. The most significant of these is a change in the age-specific incidence of BSE. In particular, the incidence in the 2- to 4-year-old age group for the first 9 months of 1992 was markedly less than the corresponding age specific incidence in 1990 and 1991. A further positive sign is that the number of weekly cases reported in 1993 is less than the corresponding number of weekly cases in 1992. In addition, the number of cattle born after the feed ban that contract BSE is much less than the number expected had there been no ban.

Although the evidence appears to support the initial hypothesis, research and epidemiologic analyses continue. All BSE cases born after the feed ban are subject to stringent epidemiologic investigation. No evidence has been uncovered to implicate either maternal or horizontal routes of transmission. A case-control study with more than 600 animals is underway to further evaluate the possible role of maternal transmission. Clinical research has so far identified only brain tissue as containing the BSE agent.

Status of BSE Risk Factors in the U.S.

The GB experience illustrates the need to recognize the potential threat of BSE and to periodically evaluate changes in potential BSE risk factors in the U.S. This evaluation will consider changes within the following risk factors: sheep demographics, scrapie status, sheep slaughter and deaths, rendering and feed manufacturing practices, and use of alternative proteins in calf milk replacers and starter rations.

Sheep Demographics in the U.S.

A brief overview of the sheep demographics in the U.S. will provide background information and may give insight into some of the factors associated with sheep scrapie. In addition, it serves to illustrate why regional differences exist in the risk of BSE within the U.S., as shown in the 1991 VS document.

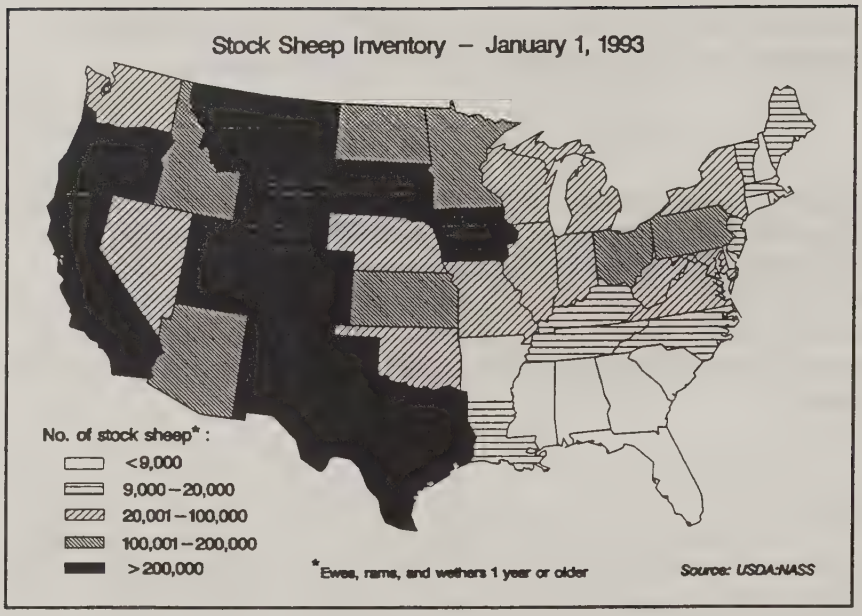

Figure 1

Stock sheep[1] 1 year and older in the U.S. totaled 6.9 million on January 1, 1993 (5), down by about 1.1 million from 3 years earlier. Western States (North Dakota to Texas and west) had 762,000 fewer sheep on January 1, 1993, representing a 12 percent decrease. Eastern States' inventory dropped by 300,600 head, a 17 percent decrease. Figure 1 shows that most of the Nation's sheep are still concentrated in the Western States, as they were in 1989.

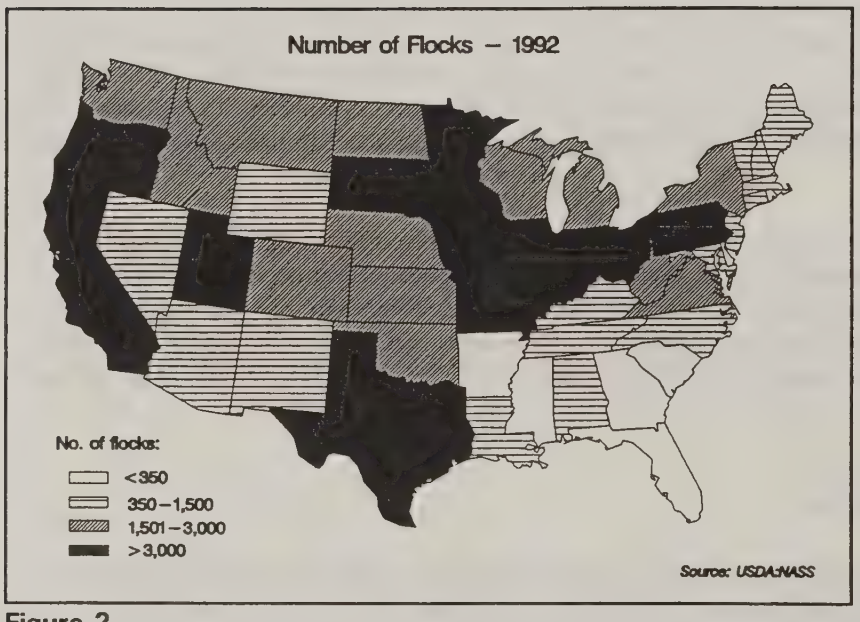

Figure 2

Figure 2 shows the number of flocks by State during 1992. Although Western States have the larger number of sheep, they have fewer flocks than many States in the Central and North Central U.S. The total number of flocks in 1992, 101,040, was a record low, down 10,000 from 1989. The geographic distribution remained the same.

The average number of sheep per flock is high in the Western States and low in the Central and North Central States (Figure 3). This distribution also has not changed since 1989.

[1] Sheep in the breeding flock, including ewes and rams used for breeding, and wethers 1 year and older

The decline in mature sheep inventory between 1989 and 1992 suggests a corresponding decrease in the potential risk for scrapie-induced BSE. Since the Eastern and Western U.S. had a proportionate decrease in numbers of sheep, it would be expected that broad regional differences in the potential risk of BSE would remain.

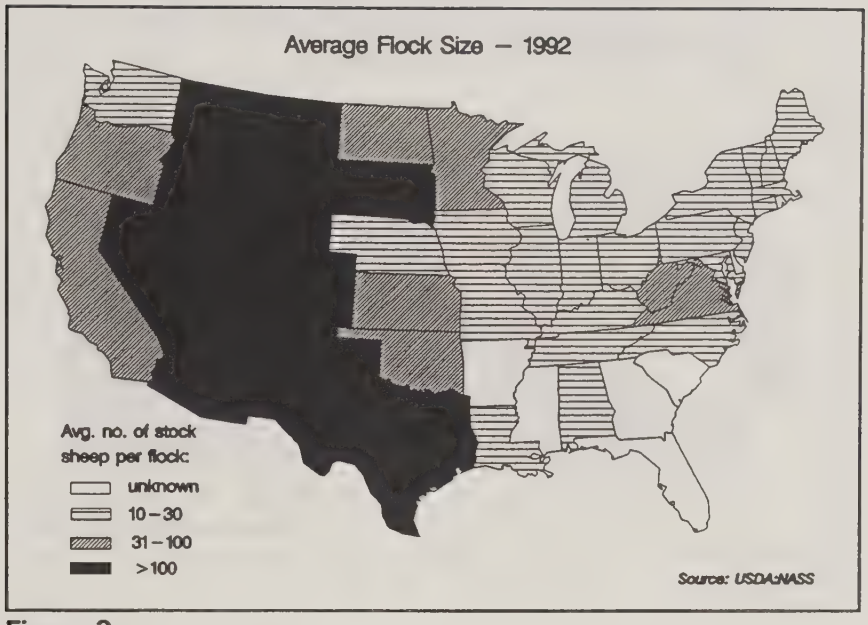

Figure 3

When evaluating the risk of BSE, it is also important to consider the mature sheep population in relationship to the population of beef and dairy cows. There were 155,000 fewer beef and dairy cows in the U.S. at the beginning of 1993 than at the beginning of 1990, representing a 0.3 percent decrease. Due to the 14 percent decline in the mature sheep population, the ratio of mature sheep to beef and dairy cows decreased slightly from 0.18 at the beginning of 1990 to 0.16 at the beginning of 1993.

Scrapie Status in the U.S.

A total of 45 newly-detected scrapie flocks were identified in 1992, as compared to 50 flocks in 1989. The distribution of newly-detected flocks was similar to that in 1989, with most of the flocks located in States with small numbers of sheep per flock (Figure 4). States with an average flock size of 30 or less had a higher ratio of newly-detected flocks to total flocks than did States with larger average flock sizes.

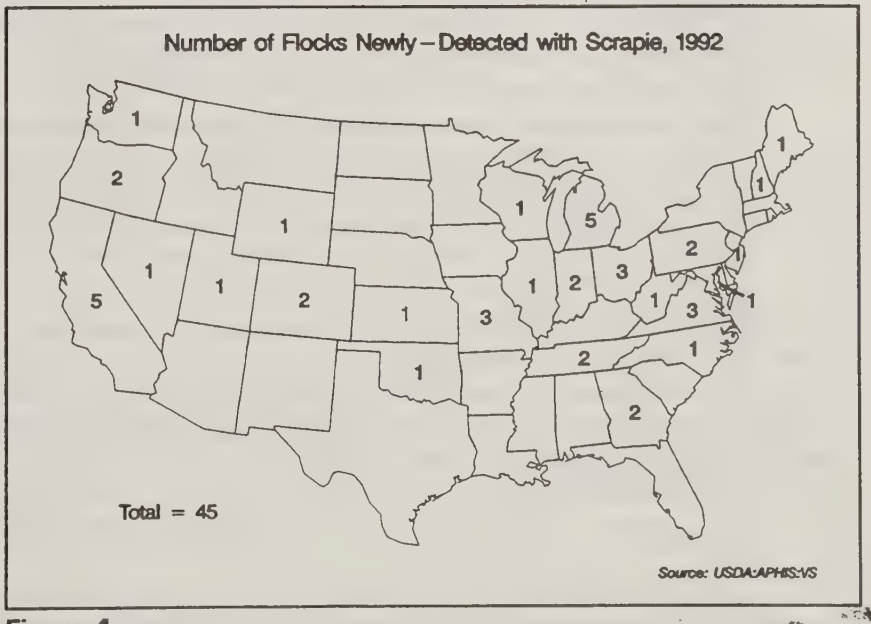

Figure 4

Various programs to eradicate scrapie have existed in the U.S. since 1952 (6). The current Voluntary Flock Certification Program was started October 1, 1992, and relies heavily on an economic incentive. Under this program, a flock can be "certified" if it is scrapie-free for a minimum of 5 years, enhancing the animals' marketability and value. Figure 5 shows the annual incidence of scrapie from 1980 through 1992. It should be

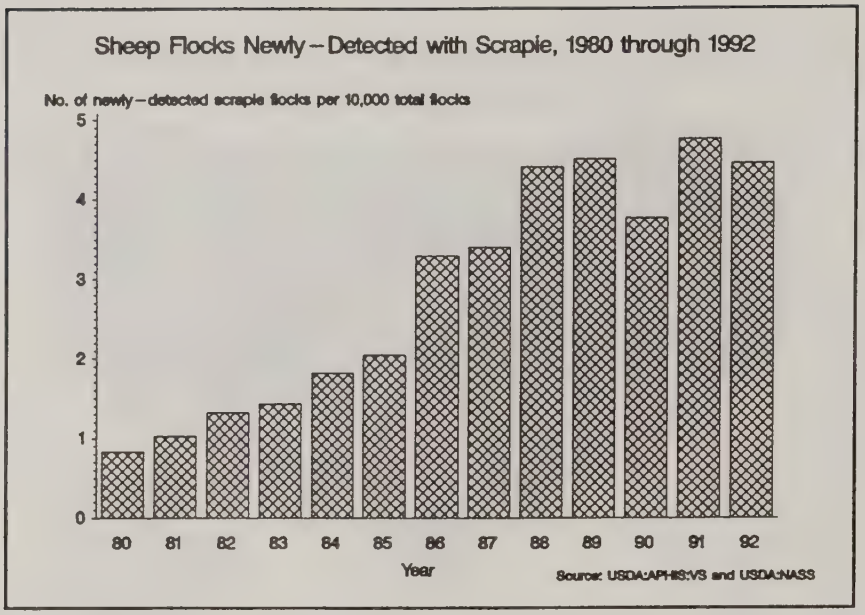

Figure 5

noted that the number of newly-reported flocks has historically varied with the amount of indemnity payment (2). Further, information on the number of infected flocks that were depopulated over the same time period was unavailable, such that changes in the prevalence of scrapie cannot be assessed. Since October 1, 1992, the USDA has approved the depopulation of about 50 infected flocks.

Sheep Slaughter and Deaths

To evaluate how the risk of BSE in the U.S. may have changed since the original assessment, it is necessary to consider changes in sheep slaughter and deaths. Table 1 shows that the total sheep inventory has dropped by almost 1.2 million head since 1989. Most of this decrease was in the category of stock sheep 1 year and older, suggesting that the downward trend may continue. Further, the number of mature sheep slaughtered in Federally-inspected plants dropped by almost 7 percent. Although there are no direct data, these figures suggest that fewer adult sheep are now going into meat and bone meal, thereby decreasing the potential risk of BSE.

Table 1
Sheep Inventory, Slaughter, and Deaths, 1992 vs. 1989

	1992	Change from 1989
Total Inventory (Jan. 1, 1993)	10,190,700	-1,177,000
Total Stock Sheep (1 year and older)	6,899,900	-1,104,600
Federally-inspected Slaughter		
Mature Sheep	330,800	-24,100
Lambs	4,719,400	-51,600
Deaths (all causes)		
Mature Sheep	439,000	-71,000
Lambs	765,000	+30,000

Federally-inspected slaughter from USDA:FSIS; all other figures from USDA:NASS

Figure 6 shows the change in number of mature sheep slaughtered in 1992 vs. 1989 for select States and the total U.S. The selected States are the 10 that slaughtered the most mature sheep in 1989. Six of the 10 States (CA, CO, IA, MN, NJ, NM) slaughtered fewer mature sheep in 1992. A total of 604 Federally-inspected plants slaughtered mature sheep in 1989, as compared to 512 plants in 1992.

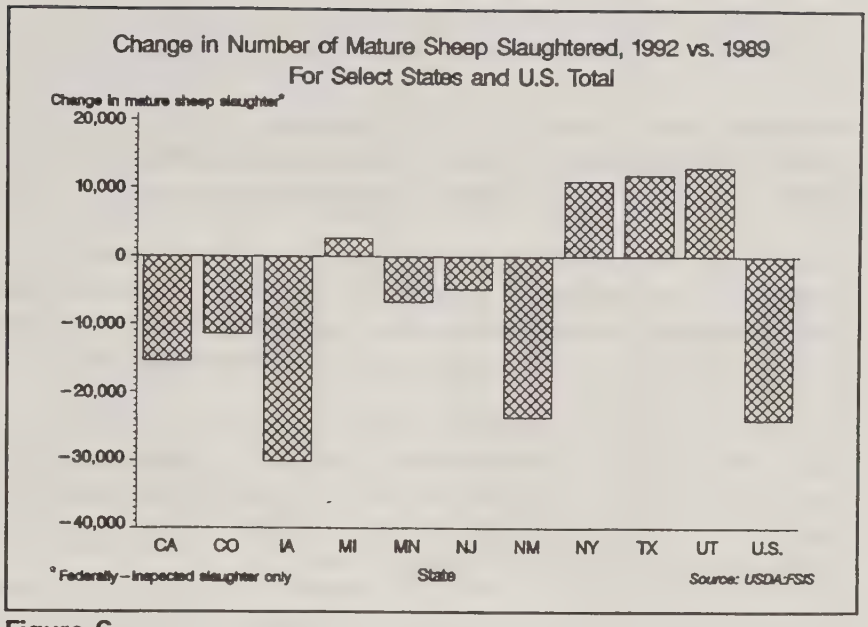

Figure 6

Rendering and Feed-Manufacturing Practices

Since practices in the rendering and feed-manufacturing industry can affect the risk of cattle contracting BSE, surveys of the two industries were conducted in 1991-92 by the American Protein Producers Industry (APPI) and the American Feed Industry Association (AFIA), respectively, in conjunction with USDA:APHIS:VS (7).

The rendering survey was sent to all 309 known renderers in the U.S. Although the overall response rate was low (38 percent), the geographic distribution and the plant size distribution of respondents were similar to the corresponding distributions of all known renderers. Responses to questions comparing rendering practices in 1985 and 1990 led to the following observations. There was a decrease in the percentage of renderers processing slaughtered mature sheep (1 year or older) from 44 percent in 1985 to 13 percent in 1990. The percent rendering heads from these sheep decreased from 42 percent in 1985 to 8 percent in 1990. The proportion of renderers processing dead sheep also decreased from 39 percent in 1985 to 7 percent in 1990. Thus, although the risk of incorporating scrapie agent in MBM decreased substantially between 1985 and 1990, it was not eliminated. Renderers continue to receive almost all of their offal from suppliers within 150 miles of the facility, and to sell approximately two-thirds of the MBM to customers within 150 miles.

The feed-manufacturers survey was mailed to 114 members of the AFIA Nutrition Council, 83 (73 percent) of whom responded. Results of the feed-manufacturing survey showed that 85 percent of the manufacturers acquired their MBM from within 150 miles, and 80 percent sold their products within 150 miles of the facility. Virtually all feed manufacturers use MBM in their feeds. Most of the MBM went into swine feed (63 percent), although 15 and 12 percent went into feeds for beef cattle and dairy cattle, respectively. Of feed products intended for dairy cattle, 53 percent included MBM from unknown species, possibly including sheep.

Information from the rendering and feed surveys generally supports a low risk of BSE in the U.S. There are, however, factors associated with both industries that allow for the possibility of sheep scrapie agent being incorporated in cattle feeds.

Alternative Proteins in Calf Milk Replacers and Starter Rations

The feeding of calf starter rations containing ruminant-origin MBM may have contributed to the magnitude and duration of the BSE outbreak in GB. A large number of calves in GB were potentially exposed to scrapie- or BSE-infected proteins through starter rations which contained MBM. The production of feed containing ruminant-derived protein was banned in GB in July 1988.

In the U.S., the use of alternative protein sources has caused some concern about calf starter rations and milk replacers. The concern is that these rations could potentially contain scrapie-infected protein from sheep products or specified bovine offal (brain, spinal cord, tonsil, thymus, spleen, and intestine from cattle over 6 months of age), which are currently banned in GB.

Of the U.S. feed manufacturers which responded to a 1992 survey, none indicated that sheep-origin MBM was used in calf starter rations (7). Those which did use MBM in such rations used beef, pork, and/or poultry as sources. It is not known if beef-origin protein contains specified bovine offal. Given available data, the risk of U.S. cattle acquiring a spongiform encephalopathy through a calf starter ration appears low.

Milk replacers in the U.S. contain an optimum of 22 percent crude protein (8,9). Neither sheep protein nor specified bovine offal are known to be incorporated into any of these products. Only muscle-derived protein of bovine and/or pork origin is sold for commercial use in calf milk replacers. Therefore, the risk of U.S. cattle becoming infected with a BSE-like agent through milk replacer consumption can be considered negligible.

Summary

A current review of BSE in the UK confirms that the course of the epidemic is consistent with the original hypothesis that MBM containing scrapie agent was incorporated into feed concentrates for cattle. Although new cases have occurred in cattle born after the July 1988 ban of specified offal in ruminant feed, almost all of those cases had access to feeds prepared prior to the offal ban. Additional new clinical cases can be expected for some time, as the mean age for onset of clinical signs is about 5 years.

Changes in sheep demographics for the U.S. since the initial BSE risk assessment in 1991 have been minimal. Inventories of stock sheep 1 year or older are down by 1.1 million from January 1, 1990. Over 24,000 fewer mature sheep were slaughtered in 1992 than in 1989. The ratio of mature sheep to beef and dairy cows is slightly lower than in 1989. The number of newly-detected scrapie flocks per 10,000 flocks has changed little since 1988.

The distribution of sheep and sheep flocks is similar to that of 1989. The largest numbers of sheep still occur in the Western States, while the largest number of flocks is in the North Central U.S. Most of the newly-detected scrapie flocks are in the eastern portion of the U.S. This may be related to husbandry practices such as sheep being kept at greater densities in the East, resulting in greater ease and more frequent observations of sheep, hence a greater likelihood of detecting sick animals. These same factors, however, could also be responsible for a higher frequency of scrapie transmission among sheep in high-density circumstances.

Practices within the rendering industry which were considered at highest risk for incorporation of scrapie agent into MBM decreased from 1985 to 1990. The procurement of offal for rendering and the distribution of MBM is generally limited to 150 miles from renderers. Most of the MBM used by feed manufacturers is obtained within a limited geographic area, and sales of feeds tend to be likewise limited. Thus the risk of scrapie agent transmission in feeds containing MBM would probably be infrequent and geographically limited.

Table 2 Summary of Risk Factors for BSE in the U.S.: 1992 vs. 1989		
Risk Factor	**Change from 1989**	**BSE Risk Compared to 1989**
Mature sheep population	Decrease	Reduction in BSE risk
Ratio of mature sheep to beef & dairy cows	Decrease	Reduction in BSE risk
Scrapie status	Voluntary flock certification program implemented	Potential reduction in BSE risk
Mature sheep slaughter and deaths	Decrease	Reduction in BSE risk
Mature sheep rendering and feed manufacturing	Decrease	Reduction in BSE risk
Protein sources for calf milk replacers and starter rations	None	No change in BSE risk

Overall, there appears to be a lower risk of scrapie-induced BSE in the U.S. today as compared to 1989 (Table 2). However, newly-identified scrapie flocks continue to occur, and practices continue in both the rendering and feed industries which allow for the possibility of sheep scrapie agent being incorporated in ruminant feeds.

References

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(2) USDA:APHIS:VS. 1991. Qualitative analysis of BSE risk factors in the United States.

(3) Walker, K.D.; Hueston, W.D.; Hurd, H.S. et al. 1991. Comparison of bovine spongiform encephalopathy risk factors in the United States and Great Britain. J Am Vet Med Assoc 199:1554-1561.

(4) Ministry of Agriculture, Fisheries and Food. December 1992. Bovine Spongiform Encephalopathy in the United Kingdom - A progress report.

(5) USDA, National Agricultural Statistics Service. 1993. Sheep and Goats. Agricultural Statistics Board. Washington, DC.

(6) USDA:APHIS. February 1991. Proposed Voluntary Scrapie Flock Certification Program.

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(8) Fowler, M. 1992. Recent calf milk replacer research update. Proceedings of the XXV American Association of Bovine Practitioners, St. Paul, MN. Vol. II:168-175.

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Bovine Spongiform Encephalopathy Surveillance in the United States

Objective

The purpose of this report is to summarize the current surveillance for BSE in the U.S. Surveillance can be divided into two main elements, targeted and general, and these, in turn, are comprised of several components. Targeted, or active, surveillance includes efforts by the U.S. Department of Agriculture (USDA) to distribute educational materials on BSE recognition and diagnosis, to monitor cattle imported from countries with BSE, and to solicit selected cattle brains for histopathologic examination. General, or passive, surveillance is based on data collected primarily by veterinary diagnostic laboratories, veterinary medical schools, and by the Food Safety and Inspection Service (FSIS) and the Animal and Plant Health Inspection Service (APHIS) of the USDA. General surveillance includes field investigations conducted by Federal veterinarians trained in the recognition and diagnosis of foreign animal diseases, and a network of private practitioners who refer unusual cases to veterinary schools and diagnostic laboratories.

Targeted Surveillance

Education

An important aspect of surveillance is the education of veterinary practitioners to recognize signs of BSE and submit specimens for definitive histopathologic evaluation. To this end, video tapes of cattle showing clinical signs of BSE have been distributed to Federal Area Veterinarians in Charge, State veterinarians, veterinary diagnostic laboratories, and pathology departments of veterinary colleges. Microscope slides showing typical BSE lesions have been sent to veterinary diagnostic and pathology laboratories, and Federal foreign animal disease diagnosticians have travelled to GB for training in BSE recognition. In addition, approximately 1,000 BSE fact sheets and 1,000 copies of a BSE risk assessment for the U.S. have been sent to State and Federal veterinarians, private practitioners, other industries, and to producers (1-3).

Such educational efforts have helped to establish an awareness of the disease by producers. The U.S. dairy industry is characterized by large, intensive operations. In 1990, 44 percent of all dairy cows were located on only 11 percent of all dairy farms (4). Such producers tend to keep themselves well-informed about industry-related topics, including diseases such as BSE.

Imported Cattle

Targeted surveillance also includes the follow-up of 459 cattle which were imported from GB and the Republic of Ireland between January 1, 1981 and July 1989. In July 1989, the U.S. prohibited the importation of ruminants from countries with BSE (5). Only four percent of the imports were dairy cattle. As of August 1992, 177 head had been slaughtered with no indication of neurologic or clinical signs suggestive of central nervous system (CNS) disorders. An additional 216 cattle had not developed signs suggestive of BSE. Sixty-six (66) of the imports could not be traced due to multiple changes in ownership subsequent to importation. Owners of imported cattle have been given BSE information and encouraged to report any signs of neurologic disease suggesting BSE.

Examination of Domestic Cattle Brains

A fundamental component of targeted surveillance entails examination of brains from adult domestic cattle with CNS disorders for neuropathologic lesions consistent with BSE. In May of 1990, USDA:APHIS issued a request for the submission of formalin-fixed brain specimens or microscope slides from BSE-suspect cattle, some of which dated back to 1986 (6). In April 1991, the scope of the investigation was expanded to include rabies-negative cattle brains. A total of 1,215 brains have been examined by the Centers for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services, USDA's National Veterinary Services Laboratories

(NVSL), and veterinary diagnostic laboratories across the U.S.

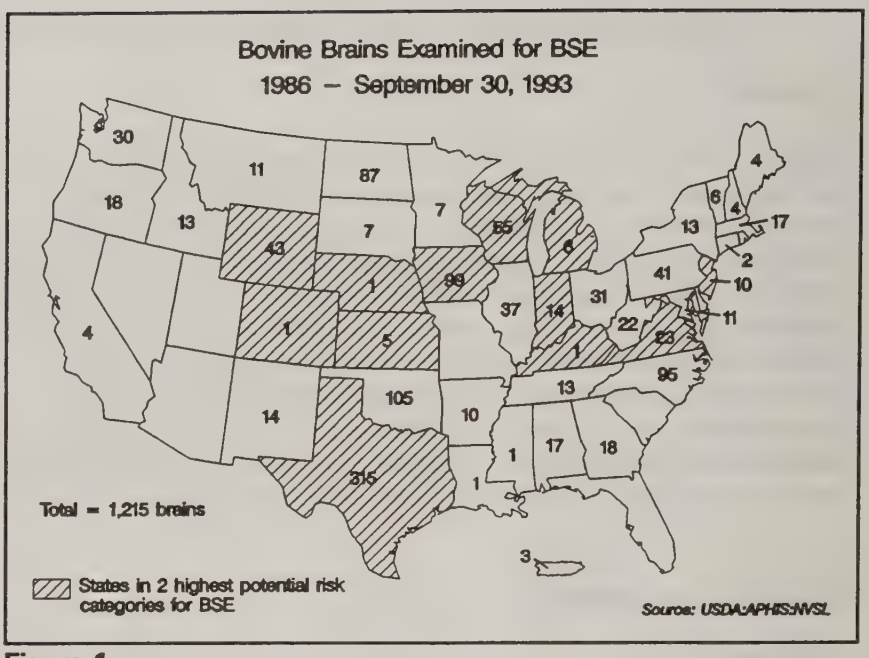

Figure 1

The largest number of specimens have come from Texas (26 percent), followed by Oklahoma (9 percent) and Iowa (8 percent) (Figure 1). All brains examined to date have been negative for BSE. The criteria by which samples were submitted for histopathologic examination have been variable. Some of the specimens were submitted for rabies diagnosis, found to be negative, and subsequently evaluated for BSE. Not all bovine brains submitted for rabies diagnosis have been examined for BSE lesions. Other cases submitted for examination were considered "BSE suspects" because they were at least 2 years old, showed signs of neurologic disease, and received protein supplement as a substantial part of their feed (6). The latter criterion was relaxed in 1992 as it was difficult if not impossible to obtain this information on some specimens received. Most samples are thought to have come from animals 2 years and older; however, little or no information was available on breed, e.g. dairy vs. beef.

Disease Prevalence and the Efficiency of Surveillance

The sample of 1,215 brains examined by the CDC, the NVSL, and veterinary diagnostic laboratories around the U.S. has been drawn from a selected population of cattle with CNS signs. However, little is known of the age, breed type, or other risk characteristics. The efficiency of such surveillance could potentially be increased by the use of more selective sampling of high-risk cattle populations as defined by the epidemiologic experience in GB.

Figure 2 illustrates the relationship between disease prevalence, sample size, and the probability of detecting disease. Note that sample size must increase in order to have the same probability of finding the disease at lower prevalences. For any fixed sample size, the probability of finding disease increases by epidemiologically defining and selecting samples from the population at highest relative risk (i.e. with a higher prevalence of disease).

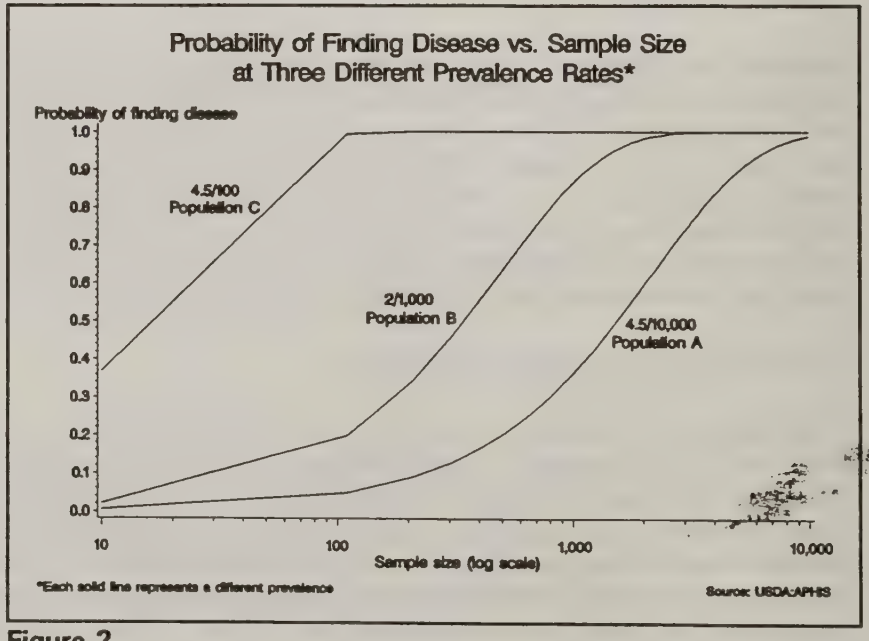

Figure 2

The three lines shown in Figure 2 represent three populations with different BSE prevalence rates. Population A represents

all cattle in Northern Ireland, which have a prevalence of BSE of about 4.5 per 10,000. Population B represents all cattle in GB, which have a prevalence of 2 per 1,000. The rate of 4.5 per 100 animals (population C) represents the prevalence of BSE in 4- to 5-year-old cattle on affected GB dairy premises containing 100 or more cows.

With a sample size of 1,215, the probability of finding disease within population A is about 40 percent. With the same sample size, the probability of finding disease within population B is almost 90 percent. By targeting the population at greatest risk (population C), sample size can be reduced to 100 and the probability of finding disease is increased to 99 percent.

Maximum Potential Prevalence of BSE

The fact that no BSE has been found in 1,215 cattle brains provides the basis for an estimate of the maximum potential prevalence of BSE in the population of adult cattle in the U.S. The population from which the 1,215 brains were sampled was adult cattle with clinical or neurologic signs suggestive of CNS disorders in the U.S. The size of this population is not known; however, results from USDA's National Dairy Heifer Evaluation Project were used to estimate that between 20,000 and 120,000 adult cows and bulls might be affected with CNS disorders each year. Because the sampling of the 1,215 brains occurred over several years and because sampling has been increased in the past 1 to 2 years, it was assumed that between 200 and 1,000 brains were examined annually. Using these figures and redefining the population to be all adult cows and bulls, the maximum potential 1-year period prevalence of BSE was estimated to range from 3.9 per 100,000 to 1.3 per million.

Research Findings Relevant to Targeted BSE Surveillance

Targeted BSE surveillance in the U.S. is based on the presumption that clinical symptoms and neuropathology would be the same as that seen in GB. Experiments performed in the U.S. have shown that calves intracerebrally inoculated with brain suspension from U.S.-origin scrapie-infected sheep will develop a BSE-like illness. However, the clinical and histological signs were different than those observed in cattle with BSE in GB (7). Although this evidence is far from conclusive, it suggests that targeted BSE surveillance in the U.S. may need to be supplemented. An important contribution would be the development of an antemortem diagnostic test based on the scrapie-associated prion protein, the focus of much current research (8).

General Surveillance

Practitioner Referrals

The network of private practitioners referring unusual cases to 60 veterinary schools or State diagnostic laboratories around the U.S. provides an extensive informal but important surveillance system. The incentive to detect and promptly report unusual findings is inherent in the competitive academic setting of such institutions, which are independent of the Federal government. No centralized data are available on the number of cattle brains examined histologically; however, inquiries to several veterinary medical schools and diagnostic laboratories showed that 20 to 30 cattle brains per institution were examined in 1992. Approximately half of these brains were from dairy cattle 2 years or older.

Foreign Animal Disease Detection

The USDA conducts many activities to detect and eliminate a foreign animal disease (FAD), such as BSE, if it were introduced. Over 200 State and Federal field veterinarians strategically located throughout the U.S., including Puerto Rico and the U.S. Virgin Islands, have been trained in the recognition and diagnosis of FAD's. Channels for reporting FAD's have been established for many years. Of 238 investigations of suspected FAD's conducted in fiscal year 1992, 16 were of animals

with encephalitides. No evidence of BSE was uncovered. The USDA trained over 100 U.S. veterinarians in FAD diagnosis in fiscal year 1992.

Veterinary School Diagnoses

Another aspect of the general surveillance system makes use of the Veterinary Medical Data Base (VMDB) maintained by Purdue University. This data base contains diagnoses submitted from 27 U.S. veterinary schools, although not all report data every year. Several neurological diagnoses[2] have no underlying etiology and may represent potential BSE cases. Figure 3 shows the rate of these neurologic diseases in cattle 2 years of age and older from 1970 to 1992. There is no evidence to suggest that the case rate has increased over the observed time period, as would be expected if the U.S. were entering a BSE epidemic. Some of the observed year-to-year variability may be due to inconsistencies in reporting by individual veterinary schools.

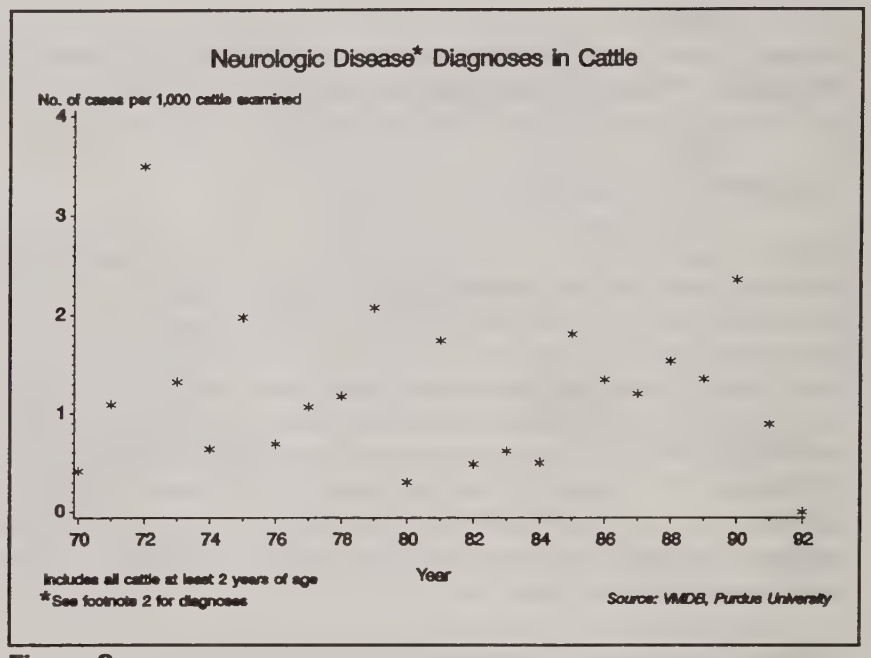

Figure 3

Antemortem Slaughter Inspection

The USDA Food Safety and Inspection Service maintains a data base of all Federally-inspected slaughter establishments, which includes antemortem condemnations due to disorders of the central nervous system. The condemnation rate due to CNS disorders in cows has increased significantly since 1983 ($p = .0006$) (Figure 4). The reasons for this trend are not known, but may include an increased awareness of CNS symptoms, especially following the identification of BSE in GB in 1986.

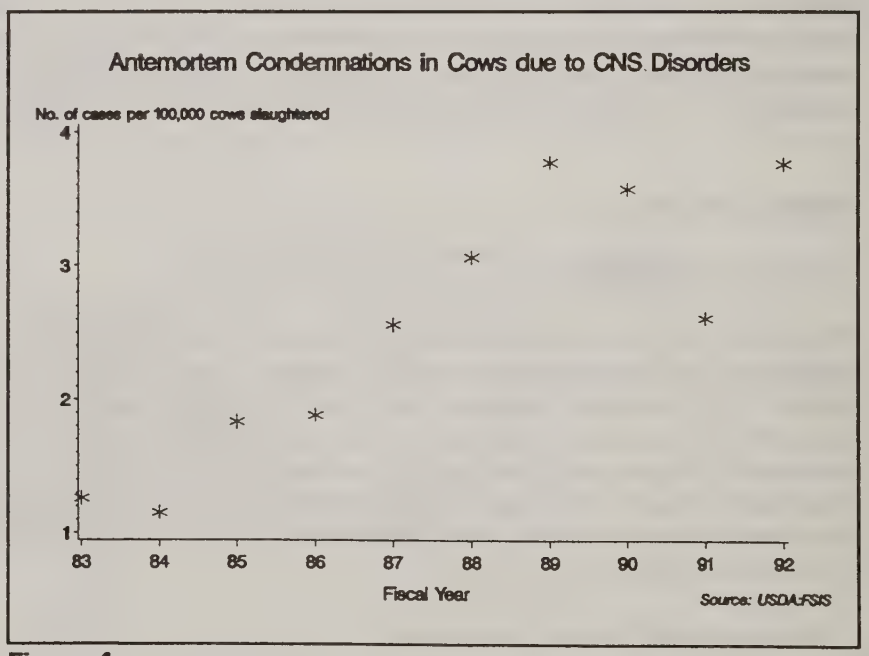

Figure 4

The same data were analyzed

[2] Degenerative nervous system; disease of nervous system due to unknown; nervous system, not specifically listed; degenerative axonopathy; encephalomyelitis; encephalomyelitis due to unknown; astrocytosis; disease of central nervous system due to unknown; axonopathy central nervous system; astrocytic swelling; hypertrophic astrocytes; degenerative neuron chromatolysis; encephalitis; encephalitis due to unknown; encephalopathy due to unknown

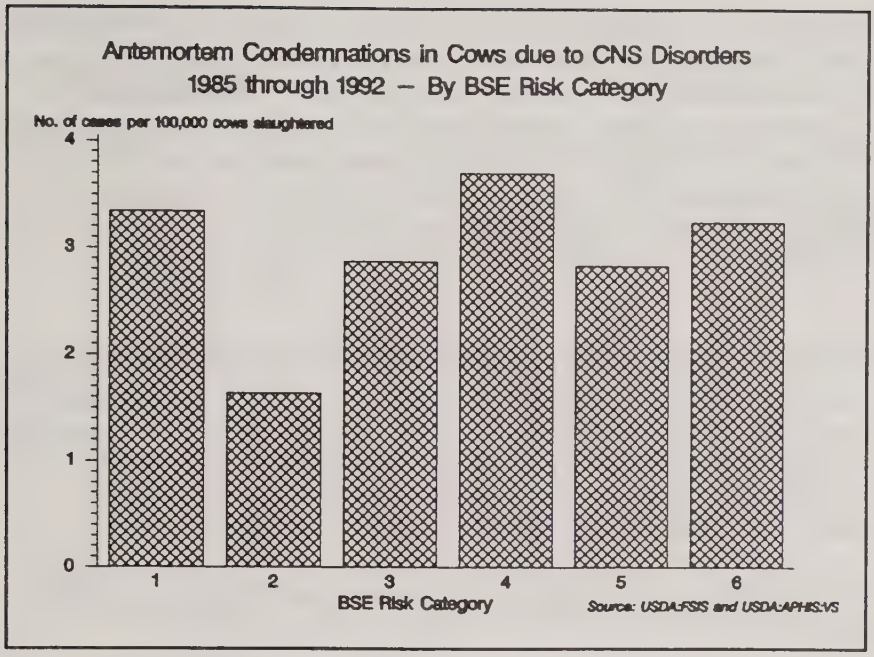

Figure 5

by BSE geographic risk categories (highest risk = category 1) as defined in a 1991 report by USDA:APHIS:VS (2) (Figure 5). There is no pattern suggesting higher rates of antemortem CNS condemnations in States potentially at highest risk for BSE. Although brains from condemned cows are currently not being examined, efforts are underway to initiate a program in which brain tissue from cattle with CNS signs received at slaughter plants are examined for BSE. In addition, nonambulatory cattle, colloquially referred to as "downers", some of which may have neurologic disorders, will be included in the surveillance efforts (9).

Veterinary Diagnostic Laboratory Reporting System

The Veterinary Diagnostic Laboratory Reporting System (VDLRS) is a cooperative effort of the American Association of Veterinary Laboratory Diagnosticians, the U.S. Animal Health Association, and USDA:APHIS:VS' Centers for Epidemiology and Animal Health. Currently 19 State and university veterinary diagnostic laboratories throughout the U.S. regularly report data to the VDLRS on a variety of diagnostic tests. Plans are underway to begin reporting numbers of histopathologic examinations of bovine brains in 1993. As a group, these laboratories examine hundreds of brains each year and are a likely point of first detection should BSE occur in the U.S.

Rabies Testing

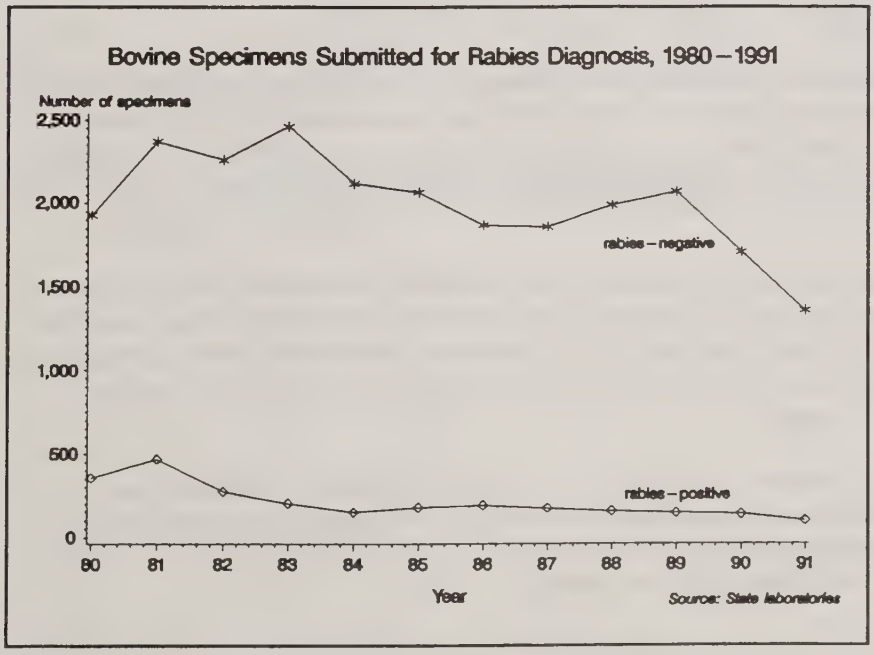

Figure 6

Brain samples from cattle with signs of neurologic disease compatible with rabies are submitted primarily to State veterinary or public health laboratories for diagnostic evaluation. There is a strong incentive to submit samples for differential diagnosis due to the consequence of human exposure to rabid animals. Because BSE and rabies have clinical signs in common, an increase in the number of rabies-negative cattle brain samples could signal an increase in the occurrence of an unrecognized CNS disease of cattle, such as BSE.

Figure 6 shows the results of rabies testing on cattle brains obtained from State public health and veterinary diagnostic laboratories for 1980 through 1991. The number of cases of wildlife rabies for four species (bats, skunks, foxes, and raccoons) was obtained from the CDC. A model was developed which looked for recent increases in rabies-negative cattle brain submissions independent of rabies in cattle and wildlife. No increase in negative cattle submissions over time was found (B. Wagner, USDA:APHIS:VS, personal communication). Thus, the evidence does not indicate an increase in undiagnosed CNS disease as measured by rabies submissions.

Zoos

BSE-like illness is not known to exist in U.S. zoos. However, scrapie-like encephalopathies have been diagnosed in five species of exotic Bovidae at zoos in Southern England (10-14). All cases were coincident with the BSE epidemic in GB's domestic cattle population, and all but one case had known or likely dietary exposure to rations containing ruminant-derived meat and bone meal. The latter case was an offspring of an index case. In this 19-month-old greater kudu, there was no dietary exposure to BSE and no direct contact with other ungulates; thus, maternal BSE transmission was suspected (14). The spongiform encephalopathy cases in GB's exotic bovids have occurred in younger animals and the disease has been of shorter duration, suggesting that these species may be more susceptible (13).

Veterinary pathologists at the major zoos in the U.S. routinely examine the brains of cases exhibiting neurologic signs. In addition, all animals that die at major zoos usually undergo necropsy in compliance with guidelines of the American Association of Zoological Parks and Aquariums. A records search conducted by two major zoos showed that no fatal diseases with unexplained clinical signs or presenting signs suggestive of spongiform encephalopathy had occurred since the onset of computerized record keeping in 1964 and 1975, respectively, (W. Heuschele, San Diego Zoological Gardens, and R. Montali, National Zoological Park, personal communication).

Summary

Surveillance for BSE in the U.S. is comprised of many components. Targeted surveillance includes examination of cattle brains by State veterinary diagnostic laboratories and the NVSL. Educational materials distributed by the USDA to diagnostic laboratories and pathology departments in veterinary schools are an often overlooked but important facet of establishing effective surveillance for BSE. Educational efforts have also generated widespread interest in and knowledge of BSE among private veterinary practitioners and producers in the U.S. dairy industry.

Based on what is known of BSE currently, histologic examination of brain specimens from cattle will be most effective when samples are selected from known high-risk groups such as dairy cattle 4 years and older from large herds. Consideration should also be given to the possibility that should BSE occur in the U.S., the neuropathologic and clinical characteristics may not be the same as those seen in GB.

General surveillance takes advantage of already existing data sources. Included in this are data on neurologic diagnoses in cattle from the VMDB (Purdue), CNS antemortem condemnation data from USDA:FSIS, necropsies performed in zoos, and the VDLRS initiative. An added benefit is that these data have been collected for many years and from many sources covering the entire country, allowing for temporal and spatial analyses.

Referral of suspect clinical cases by private practitioners to veterinary teaching hospitals and diagnostic laboratories provides widespread surveillance in the U.S. The importance of this network of clinicians and diagnostic laboratories to detect BSE is critical. Foreign animal disease diagnosticians form an important complement to this network.

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A Quantitative Assessment of the Possible Role of Nonambulatory Cattle in Transmissible Spongiform Encephalopathy in the United States

Background

The emergence of bovine spongiform encephalopathy (BSE) in Great Britain and other countries has focused attention on certain cattle populations in the U.S. One such population is nonambulatory cows. The term nonambulatory cow (or "downer" cow) refers to any cow that is recumbent when the reason for the recumbency is unknown (1,2). Some researchers feel that nonambulatory cows occur secondarily to low blood levels of calcium (2,3), while others suggest that nonambulatory cows occur as a sequela to prolonged recumbency due to a variety of other causes (e.g., mastitis, metritis, calving paralysis, and milk fever) (4). Though many causes for nonambulatory cows have been proposed, most studies have failed to find evidence of any of these conditions in a large fraction of the nonambulatory cows. Nonambulatory cows are alert and unresponsive to therapy if treated. Terminal cows due to a known disease are not considered nonambulatory. For the purpose of this report, the term nonambulatory cow refers to a cow that is culled because it is unable to stand.

BSE is a neurologic disorder that affects cattle. BSE has occurred in seven countries, and is believed to have been initiated through the feeding of meat and bone meal contaminated with sheep scrapie. BSE is not known to exist in the U.S., but it has been suggested that an unidentified transmissible spongiform encephalopathy (TSE) may be present in U.S. nonambulatory cows (5). This hypothesis is based on an alleged association between feeding nonambulatory cattle to mink and outbreaks of transmissible mink encephalopathy (TME) (6,7). There have been five reported outbreaks of TME in the United States; one in 1947, three in the early 1960's, and one in 1985. The outbreaks in the early 1960's were associated with common food sources and movements between farms (8). The large fraction of nonambulatory cases that are due to unknown cause provides a basis for the hypothesis that a TSE may exist in U.S. cows and be a source of TME. The purpose of this report is to describe the occurrence and disposition of nonambulatory cows in States with both dairy and mink industries, and to assess the potential role of these cattle in the transmission of a spongiform encephalopathy.

Nonambulatory Cow Prevalence and Disposition

The prevalence of nonambulatory cattle in the U.S. is difficult to estimate due to the numerous options for disposition of such animals. Nonambulatory cows may go to Federal or State slaughter plants, to rendering plants, be custom slaughtered, sold locally, or killed and disposed on the premises (Figure 1). Of particular interest are the number sold locally to mink producers. The greatest number of nonambulatory cows are believed to go to rendering. Rendering facilities do not maintain records on numbers and causes of nonambulatory cows as nonambulatory cows represent only a small fraction of incoming rendered product,

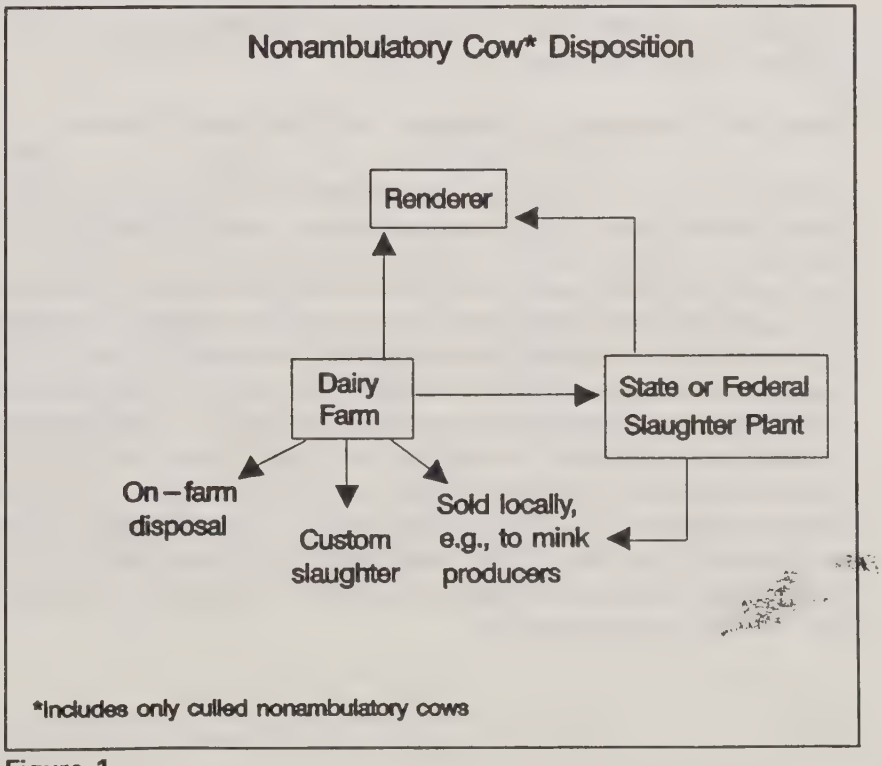

Figure 1

and acquisitions are made by drivers who are not trained nor charged with responsibility to assess reasons for moribundity.

Three sources of information on the prevalence and disposition of nonambulatory cows were utilized for this report: a review of the literature; State-inspected slaughter plants that slaughter nonambulatory cattle exclusively; and a survey to determine incidence and disposition patterns at the farm level.

Literature Review

The reported incidence of nonambulatory cows varies with the definition used. The annual incidence of nonambulatory cows was 21.4 per 1,000 cow-years at risk, in dairy herds participating in the Dairy Herd Improvement Association in Minnesota in 1983. Cows unable to stand for no obvious reason, including those that eventually recovered, were considered to be nonambulatory (1). A prospective study of 34 dairy herds in New York revealed that 28 nonambulatory cow cases occurred out of 7,763 lactations (4,092 animals) during a 4-year period, or 3.6 per 1,000 cow-years at risk (9). For that study, cows that recovered were not reported as nonambulatory.

Concerning disposition of nonambulatory cattle, Milian-Suazo et al. (10) reported that more than one-half of nonambulatory cows were culled in the same lactation. It has also been reported that some mink ranchers have contracts with local slaughter plants to pick up nonambulatory or dead cows (8). The entire carcass is reportedly ground into feed at the mink facility.

Antemortem Slaughter Inspection in Federal and State Plants

One possible endpoint for nonambulatory cows is a Federal or State slaughter plant. The United States Department of Agriculture: Food Safety Inspection Service (USDA:FSIS) maintains a record of animals condemned antemortem due to a variety of reasons, but there is no category specifically for nonambulatory cows. State-inspected slaughter plants may also accept nonambulatory cows. The only available data on nonambulatory cows from State plants came from Wisconsin, which has the largest number of milk cows in the U.S. and has four State-inspected plants specifically for nonambulatory cows. In 1992, these four plants slaughtered a total of about 10,000 nonambulatory cows (G. Jacobsen, AVIC, USDA:APHIS:VS, personal communication). Neither the number of cows that were condemned antemortem and not slaughtered nor the slaughtered cows' State of origin was known.

Farm-level Information on Numbers and Disposition Patterns

Because data from slaughter were limited and do not capture the fraction of nonambulatory cows going directly from farm to mink producer, a survey was conducted to determine the incidence and disposition of nonambulatory cows at the farm level. Sampling was from States with both dairy and mink industries, and was not random. Seven States were selected based on geographic distribution and ranking by numbers of milk cows and mink bred. Twenty-one dairy practitioners were selected from lists provided by university faculty, dairy organizations, and USDA contacts. Each practitioner was asked to select three herds to sample for the study, one from each of three size categories (small $n \leq 50$; medium $51 < n \leq 100$; and large $n > 100$) . The number of practitioners selected for each State was calculated based on the number of dairy cows per State. Eight practitioners were contacted in Wisconsin; four in New York; three in Pennsylvania; three in Minnesota; and one each in Idaho, Utah, and Washington. Eighty-one percent (17/21) of the practitioners responded. The response rate by State was 100 percent for New York, Pennsylvania, Wisconsin, and Idaho; 33 percent for Minnesota; and 0 percent for Washington and Utah. A total of 51 herds was represented.

Incidence of Nonambulatory Cows in the Study Sample

Responding veterinarians reported 363 nonambulatory cows out of 13,429 cows on the 51 premises for 1990-1992, for an incidence of 27 per 1,000 cow-years at risk. Incidence of nonambulatory cows was 35, 21, and 28 per 1,000 cow-years at risk for small, medium, and large herds, respectively. There was no evidence of regional differences in rates of nonambulatory cows.

Only those cattle without identifiable reasons for being nonambulatory have been hypothesized as potentially having a TSE. The incidence of nonambulatory cows of unknown cause reported in the study sample for 1992 was 8 per 1,000 cow-years at risk. Nonambulatory cows of unknown cause accounted for 22.8 percent of all nonambulatory cows. Incidence for nonambulatory cows of unknown cause in 1992 was 12, 5, and 8 per 1,000 cow-years at risk for small, medium, and large herds, respectively.

Disposition of Nonambulatory Cows in 1992

For 1992, there were 158 nonambulatory cows reported in the study sample. The initial disposition of more than half of the nonambulatory cows was rendering (Table 1). Most of the remaining nonambulatory cows initially went to slaughter, with those condemned at slaughter potentially going to rendering or to mink producers. Of the 6.3 percent of nonambulatory cows that went directly to mink producers, half had no identifiable reason for being nonambulatory.

Table 1
Initial Disposition of Nonambulatory Cows from 51 Dairies in 1992

Disposition	Number	Percent*
Renderer	83	52.5
Regular Slaughter	45	28.5
Mink Producers	10	6.3
Dealer	10	6.3
Custom Slaughter	9	5.7
Livestock Market	1	0.6
Total	158	100.0

* Totals may not add due to rounding

There was no correlation between distance to disposition site and method of disposition. The average distance from a herd to: the nearest slaughter plant was 29 miles; the nearest renderer was 25 miles; and the nearest mink ranch was 36 miles.

Nonambulatory Cattle as a Potential Source of TSE

In this study, Wisconsin was the only State in which mink producers were reported to receive nonambulatory cows directly from dairies. However, given the small number of surveyed herds this finding is likely a result of the sampling design. Because mink producers pay a premium for nonambulatory cows, it appears reasonable that the practice of feeding nonambulatory cows to mink could occur wherever both large numbers of dairy cows and mink are found. As many as 2,157[3] nonambulatory cows per million milk cows, or a total of 9,482 nonambulatory cows, could have been fed to mink in the 7 surveyed States in 1992. Based on the sample response, only half of those cows would have had an identifiable reason for being nonambulatory. This equates to an estimated 4,741 nonambulatory cows that were, hypothetically, a potential source of TSE in the surveyed States.

[3]This estimate does not account for any nonambulatory cows received from slaughter plants.

The five reported outbreaks of TME in the U.S. reveal no discernable trend. Assuming an average of 2,000 mink farms in the U.S. during the last 50 years, one outbreak of TME has occurred per 20,000 mink farm-years. Extrapolating from the data gathered in this study, 66,374 nonambulatory cows have been fed to mink in the 7 surveyed States since the last reported outbreak of TME in 1985. Of those, 33,187 would have had no identifiable reason for being nonambulatory and were hypothetically a potential source of TSE. Given the severity of signs and number of mink affected by TME it is unlikely that outbreaks have gone unreported. If any form of a TSE (infectious, spontaneous, or other) occurs in U.S. cattle that is transmissible to mink in the form of TME, then it must be exceedingly rare or the conditions for its transmission must be highly specific and unusual. Nonetheless, studies are underway at the State and Federal levels to further characterize the disposition of nonambulatory cows and usage on mink farms.

Summary

Little attention has been given to nonambulatory cows in the past. The emergence of BSE and TME has brought the issue of nonambulatory cows into focus. Limited information is available on the numbers and disposition of nonambulatory cattle in the U.S. Available estimates vary greatly, depending on how the condition is defined. Federal and State slaughter plants provide information on antemortem condemnation rates due to a variety of reasons, but no data exist that capture all nonambulatory cows.

Data from a nonrandom survey of dairy herds in States with mink were used to estimate the incidence of nonambulatory cows between 1990 and 1992. In surveyed herds, the incidence of nonambulatory cows was 27 per 1,000 cow-years at risk. In 1992, the incidence of cows which were nonambulatory for no obvious reason was 8 per 1,000 cow-years at risk. Over half of the nonambulatory cows reported went to rendering. Most of the remaining nonambulatory cows initially went to slaughter and 6.3 percent went directly to mink.

An estimated 4,741 nonambulatory cows hypothetically considered to be potential sources of TSE may have been fed to mink in the 7 surveyed States in 1992. This equates to 33,187 such cows fed to mink since the last reported outbreak of TME in mink. Given this large number of nonambulatory cows fed to mink, the historic and current mink population, and the infrequent occurrence of TME, if TSE exists in cattle in the U.S. it must be very rare or transmissible to mink only under very unusual conditions.

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